conversion at base 197 and comprises bases 182-202 of the sense strand of the 491 bp fragment. The M4 primer is a 21 base antisense (-) oligonucleotide (5'-ACCCTCTGAAGGCTCGAGTTC-3') (SEQ ID NO:85) that has a C>G conversion at base 197 of the antisense strand and comprises bases 212-192 of the antisense strand of the 491 bp fragment. The initial amplification with CF1/M4 and M3/CF5 gives fragments that are 212 and 310 bp, respectively for the wtCFTR sequences. For ΔF508 CFTR the fragments are CF1/M4 (212 bp) and M3/CF5 (307 bp), since the ΔF508 mutation deletes bases 293-295 of the 491 bp wtCFTR fragment. Restriction digestion of the 491 bp or 488 bp fragments with Xho I yields digestion fragments of 199 bp and 292 or 289 bp, respectively.

IN THE CLAIMS

Please cancel claims 8-16 without prejudice to further prosecution, and add new claims 17-40 as follows:

17. (NEW) A method for replacing a target fragment of a gene in a cell, the method comprising delivering to the cell an exogenous replacement DNA fragment, the replacement DNA fragment consisting essentially of:

(a) at least one replacement exon having a 3' end and a 5' end;

(b) a 3' end consisting essentially of a 3' flanking intronic sequence adjacent to the 3' end of the at least one replacement exon; and

(c) a 5' end consisting essentially of a 5' flanking intronic sequence adjacent to the 5' end of the at least one replacement exon;

wherein the 3' flanking intronic sequence of the replacement DNA fragment is homologous to and anneals to a 3' flanking intronic sequence adjacent to the target fragment, and the 5' flanking intronic sequence of the replacement DNA fragment is homologous to and anneals to a 5' flanking intronic sequence adjacent to the target fragment, so that the exogenous replacement DNA fragment replaces the target fragment of the gene in the cell.

18. (NEW) The method of claim 17, wherein the cell is *ex vivo*.

19. (NEW) The method of claim 17, wherein the cell is *in vivo*.

20. (NEW) The method of claim 17, wherein the target fragment of the gene in the cell comprises a DNA sequence comprising a genetic defect that controls a disease or dysfunction.

21. (NEW) The method of claim 20, wherein the disease or dysfunction is Fanconi's anemia, cystic fibrosis, sickle cell anemia, thalassaemias, retinitis pigmentosa, xeroderma pigmentosum, ataxia telangiectasia, Bloom's syndrome, retinoblastoma, Duchenne's muscular dystrophy, or Tay-Sachs disease.

22. (NEW) The method of claim 20, wherein the target fragment of a gene is a DNA sequence present in the cystic fibrosis gene.

23. (NEW) The method of claim 20, wherein the target fragment of a gene is a DNA sequence present in the sickle cell anemia gene and the target fragment is replaced with a replacement genomic DNA sequence encoding β-globin.

24. (NEW) The method of claim 20, wherein the targeted mutant DNA sequence is a DNA sequence present in the gene causing thalassaemias, wherein the sequence is replaced with a replacement genomic DNA sequence in the thalassaemias causing genomic loci.

25. (NEW) The method of claim 20, wherein the targeted mutant DNA sequence is a DNA sequence present in a gene causing xeroderma pigmentosum.

26. (NEW) The method of claim 17, wherein the DNA is single stranded.

27. (NEW) The method of claim 17, wherein the DNA is double stranded.

28. (NEW) The method of claim 17, wherein the delivering of the exogenous replacement DNA fragment comprises delivery by electroporation, microinjection, complexing the exogenous

replacement DNA fragment onto a lipid layer, complexing the exogenous replacement DNA fragment in a dendrimer or conjugating the exogenous replacement DNA fragment to polylysine.

29. (NEW) The method of claim 17, wherein the method is directed at a population of cells containing the target fragment of the gene, and further comprising determining the extent of homologous replacement by PCR identification of cells within the population that have replaced the target fragment of a gene with the exogenous replacement DNA fragment at a target genomic locus.

30. (NEW) The method of claim 29, wherein the exogenous replacement DNA fragment is identified using primers of about 25 bases that are outside of regions of homology defined by the exogenous replacement DNA fragment, or primers that are allele-specific and differentiate between the target fragment of a gene and the exogenous replacement DNA fragment, or by Southern hybridization with allele-specific oligonucleotide probes that differentiate between the target fragment of a gene and the exogenous replacement DNA fragment.

31. (NEW) The method of claim 17, wherein the exogenous replacement DNA fragment is uncoated or coated with a recombinase or complexed with a protein, provided that the recombinase is not recA.

32. (NEW) The method of claim 17, wherein the exogenous replacement DNA fragment is generated by PCR amplification, oligonucleotide synthesis, plasmid cleavage with restriction endonuclease or by a combination of restriction enzyme cleavage of plasmid inserts and ligation of contiguous insert fragments.

33. (NEW) The method of claim 32, wherein the PCR amplification is performed with primers specific for the exogenous replacement DNA fragment.

34. (NEW) The method of claim 33, wherein the target fragment of a gene is a DNA sequence present in the cystic fibrosis gene, and the primers are selected from the group consisting of primers CF1, CF1B, CF5, CF6, CF7B, CF8B, CF7C, CF8C, CF9, CF14, CF17 and CF22.

35. (NEW) The method of claim 33, wherein the target fragment of a gene is a DNA sequence present in the sickle cell anemia gene, the target fragment is replaced with a replacement genomic DNA sequence encoding β-globin, and the primers are selected from the group consisting of primers SC1(+), SC2(-), SC3(+), SC4(-), SC5(+), SC6(-), SC-BA(-) and SC- BS(-).

36. (NEW) The method of claim 17, wherein the exogenous replacement DNA fragment is from 1 to about 2000 bases.

37. (NEW) A composition comprising a replacement DNA fragment and a delivery vehicle suitable for delivery of the replacement DNA fragment into a cell containing a target fragment of a gene, wherein the replacement DNA fragment consists essentially of:

(d) at least one replacement exon having a 3' end and a 5' end;

(e) a 3' end consisting essentially of a 3' flanking intronic sequence adjacent to the 3' end of the at least one replacement exon; and

(f) a 5' end consisting essentially of a 5' flanking intronic sequence adjacent to the 5' end of the at least one replacement exon;

wherein the 3' flanking intronic sequence of the replacement DNA fragment is homologous to and anneals to a 3' flanking intronic sequence adjacent to the target fragment, and the 5' flanking intronic sequence of the replacement DNA fragment is homologous to and anneals to a 5' flanking intronic sequence adjacent to the target fragment, so that the exogenous replacement DNA fragment replaces the target fragment of the gene upon delivery of the replacement DNA fragment into the cell.

38. (NEW) A method for gene therapy comprising contacting a cell with the composition of claim 37 so that the replacement DNA fragment is delivered into the cell and corrects a genetic defect in the target fragment of the gene in the cell.

39. (NEW) The method of claim 38, wherein the contacting occurs *ex vivo*.

40. (NEW) The method of claim 38, wherein the contacting occurs *in vivo*.